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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,012	02/01/2005	Joachim Moormann	3868-0160PUS1	7480

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EXAMINER	
PALENIK, JEFFREY T	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
02/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,012	MOORMANN ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11,13-16 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *10,11,13-16,18,19 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8,9,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

STATUS OF APPLICATION

Receipt is acknowledged of Applicants' remarks and amended claims filed on 16 October 2009, in the matter of Application N° 10/523,012. Said filings are entered on the record. The Examiner further acknowledges the following:

Applicants have neither added nor canceled any claims.

Dependent claim 21 alone has been amended to depend from claim 1, rather than canceled claim 2.

No new matter has been added.

Thus, claims 1, 3-6, 8, 9, 20 and 21 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been submitted for consideration.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicants' amendment to claim 21 correcting its dependency is sufficient to render moot the objection.

MAINTAINED REJECTIONS

The following rejections are maintained from the previous Office Correspondence dated 16 July 2009 since either the grounds or art on which they were previously set forth continues to read on the amended limitations.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Plata-Salaman (US Pre-Grant Publication N° 2003/0060423) and Moormann (USPN 5,643,905).

The instantly amended claim 1 is directed to a composition "characterized" by (e.g. comprising; see MPEP §2111.03) of two administration forms: 1.) an administration form that continuously releases at least one modulator of nicotinic receptors selected from galanthamine or one of its salts, and 2.) an administration form which enables a rapid entry of galanthamine or one of its salts in to the Central Nervous System, wherein the second form is further limited to one of the following routes of administration: buccal (i.e. sublingual) solutions, spray solutions or drip solutions (claim 1). The dependent claim 3 further limits the continuous release administration form to transdermal therapeutic systems, subcutaneous implants or intramuscularly injectible preparations. Claim 4 further limits the composition of claim 3 such that the intramuscularly injectible preparation is a suspension of microcapsules containing the modulator(s). Claim 20 further limits claim 1 such that the two dosage forms are administered independently.

Regarding the forgoing limitations, the Plata-Salaman reference expressly teaches co-therapy compositions comprising a therapeutically effective amount of one or more acetylcholinesterase inhibitors ¶¶[0018] and [0071], such as galanthamine ¶¶[0055] and [0056]. The term "co-therapy," as defined in ¶[0033], refers to at least one compound of a general "formula I" being administered with at least one acetylcholinesterase inhibitor wherein said

compound(s) and inhibitor(s) are administered simultaneously, sequentially, separately or in a single pharmaceutical formulation. Instances where dosing does not occur in a single formulation, the routes of administration may be varied and include: intramuscular, transdermal, subcutaneous, as well as being directly applied to the nervous system. Topical, intranasal administration of the active agent is also taught ¶[0076]. Unit dose forms such as tablets, pills, and capsules, each of which include immediate-, timed-, and sustained release formats, are taught ¶[0072]. Additional dosing systems and formats such as injected (e.g. parenteral) suspensions, metered liquid sprays, drops, ampoules, and autoinjector devices are taught [0072], each of whose design is capable of incorporating distribution nozzles.

Plata-Salaman does not teach galanthamine or any of its salts as being the sole medicament of either the immediate or continuous release formulations. Nor is the intended use of treating addictions using galanthamine expressly discussed. However, the teachings of Moormann cure these deficiencies.

Moormann expressly teaches using galanthamine and the pharmaceutically acceptable salts thereof for the treatment of an addictive craving such as nicotine dependence (Abstract). It is further expressly suggested that galanthamine may also be used to treat alcohol withdrawal (col. 2, lines 62-64). Regarding forms of administration with which galanthamine may be delivered, Moormann expressly teaches that continuous and controlled delivery methods include oral, transdermal and parenteral modes (Abstract). The term "parenteral" is further defined as including application forms which exclude the oral form, such as intramuscular and nasal forms of administration (col. 2, lines 1-8).

Though both continuous and immediate forms of administration are expressly taught, the teachings of Moormann are deficient regarding the combined, but separate administration of galanthamine.

However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to have prepared a combined yet sequential administration form consisting of galanthamine or one of it salts as instantly claimed. The ordinarily skilled artisan would have been highly motivated to prepare the instantly claimed composition, particularly since galanthamine-based formulations are capable of being separately co-administered (e.g. sequentially) as both a continuous form and as an immediate oral or nasal solution form as clearly taught by Plata-Salaman. Further motivation is provided by Moormann who expressly discusses a method for treating nicotine dependence using galanthamine (claims 1-4).

Based on the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable high expectation of successfully producing simultaneously administered separate dosage forms consisting of galanthamine for treating addiction. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, alone or in combination, especially in the absence of evidence to the contrary.

Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Plata-Salaman, with respect to claims 1, 3 and 4, as set forth above.

Claim 5 further limits the continuous release administration form to either release between 10 and 25 mg of galanthamine or a pharmaceutically acceptable salt of it, per day, whereas claim 6 further limits the quick entry administration form of the composition such that it contains 1 to 5 mg of galanthamine or a pharmaceutically acceptable salt of it.

Regarding the teachings of Plata-Salaman, paragraph [0070] further expressly teaches that galanthamine is administered in an amount in the range of about 2 to about 32 mg daily and more preferably from about 4 to about 24 mg once or twice daily. The paragraph further teaches that Reminyl®, which is the unit dose tablet form of galanthamine, may be administered in a 12 mg dose.

Though amounts of galanthamine are taught, which would encompass the total amount of drug administered by the combination of the co-administered dosage forms, as claimed by Applicants, it is not expressly taught how much galanthamine is formulated into either of the dosage types. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. For example, Plata-Salaman expressly discusses that multiple dosage types and routes may be employed to deliver a total of 2-32 mg of galanthamine daily ¶¶[0070] and [0072]. Thus, it would have been customary for an artisan of ordinary skill, to adjust the formulated amount of galanthamine administered continuously as well as rapidly (e.g. nasally) in the composition, particularly in view of ¶¶[0070] and [0072], in order to achieve the desired delivery format. Thus, absent some

demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejections of claims 1, 3-6 and 20 under 35 USC 103(a) as being unpatentable over the combined teachings of Plata-Salaman et al. and Moormann et al. have been fully considered but they are not persuasive.

Applicants allege that the invention of Plata-Salaman teaches away from the instant invention on the grounds that the definition of the term "co-therapy" "clearly indicates … the administration of two different pharmaceutically active substances selected from different groups of drugs", namely an anticonvulsant and an ACE inhibitor, and that the reference does not indicate that "co-therapy" means the simultaneous, sequential, or separate administration of the same active by different administrative forms.

First, in response to Applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Secondly, the definition of "co-therapy" as employed by Plata-Salaman at ¶[0033] teaches that a patient may be treated through the administration of one or more compounds of formula I with one or more acetylcholinesterase inhibitor compounds, wherein said compounds are administered in such manners as sequentially, simultaneously, separately or in a single dosage form. The modes of administration are expressly taught as being oral, intravenously,

intramuscular, subcutaneous, transdermal, and rectal. It is further expressly taught that both the one or more formula I compounds and the one or more ACE inhibitors may be administered via the same or different routes of administration. It is therefore expressly taught, if not suggested that multiple dosages of an ACE inhibitor may be administered to a patient and by different administration routes, such as those which are instantly claimed. Concerning the point that Plata-Salaman teaches co-administration with an active substance of a different class (e.g., anticonvulsant), the Examiner respectfully reminds Applicants that the instant invention recites "comprising" language and that such language does not preclude the use of other elements in order to anticipate, teach or suggest the instant invention (see MPEP §2111.03).

Furthermore, the teachings of Plata-Salaman are interpreted by the Examiner as providing a finite number of options which are well known in the art and thus well known to an artisan of ordinary skill. A person having ordinary skill in pharmaceutical research, under the guidance of the Plata-Salaman reference, would have been able to arrive at an administration scheme wherein more than one dose of an ACE inhibitor such as galanthamine could be administered separately and/or sequentially by different routes of administration. Clearly, the ordinarily skilled artisan would have immediately recognized that the advantage to doing so lay in achieving multiple types of release (i.e. combined immediate and sustained releases) for the ACE inhibitor. An additional advantageous result to such an administration scheme is that the administration need only take place once a day and last all day. Said recognition constitutes a combination of prior art elements in accordance with known methods in order to yield predictable results and thus provides the necessary motivation to the ordinarily skilled artisan to modify the teachings of Plata-Salaman to arrive at the instantly claimed invention (MPEP §2141). Thus, Applicants'

remarks regarding "impermissible 'obvious to try' analysis", while having been fully considered by the Examiner, are unpersuasive.

Applicants secondarily assert that the Moormann reference fails to remedy the deficiencies of the Plata-Salaman reference on the grounds that galanthamine is used to treat completely different conditions in each of the references. Moormann, the older of the two references, discloses the use of galanthamine for treating addictions, per the instant claims, whereas Plata-Salaman discloses its use for treating behavioral manifestations such as dementia.

In response, the Examiner respectfully submits that Applicants' remarks are unpersuasive on the grounds that Applicants' are arguing the intended use of a composition. The invention is directed to a composition comprising two different administration forms of galanthamine, which the art of record clearly teaches. MPEP §2112(I) states that "claiming a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable". Further, regarding composition claims, MPEP §2112.01(II) states that "[p]roducts of identical chemical composition can not have mutually exclusive properties" and that "a chemical composition and its properties are inseparable". Thus, despite the fact that the references both teach compositions comprising galanthamine for seemingly divergent purposes, it follows that since galanthamine is well known in the art as being used to treat a given condition (e.g. addiction cravings) it is thus inseparable from that property regardless of the teaching.

For these reasons, Applicants' arguments are found unpersuasive. Said rejections are therefore **maintained**.

Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samuels (USPN 2,906,265), with respect to claim 1 as set forth above.

Claim 8 recites that the administration format for the rapid entry form is a flexible plastic container having a capacity between 1-5 mL. Claim 9 further limits claim 8 such that said plastic container is provided with nozzles through which the solution can be sprayed or dripped intranasally.

The teachings of Plata-Salaman are discussed above. Though intranasal administration of liquid sprays and drops is expressly taught ¶[0070], the actual device which contains and delivers said formulation is not expressly discussed.

However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to have used a flexible plastic container having a nozzle in order to intranasally deliver the instantly claimed galanthamine formulation. The ordinarily skilled artisan would have been highly motivated to do so and reasonably would have expected success because such containers are extremely well-known in the prior art. Such is evidenced, for example, by the teachings of Samuels which are directed to nasal adaptor devices which comprise a nozzle and a base portion (col. 1, lines 50-53). The practiced device is preferably constructed from flexible plastic (col. 2, lines 33-34) and may function to either drip or spray the contained formulation into the nose (claims 1 and 4). The format and parameters of such devices (e.g. containment volume), while not expressly taught, are well within the purview of the skilled artisan to optimize. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of the rapid-release dosage container would have been obvious at the time of Applicants' invention.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection of claims 8 and 9 under 35 USC 103(a) as being unpatentable over the teachings of Samuels et al., with respect to claim 1, have been fully considered but they are not persuasive.

Applicants allege that the Samuels reference does not remedy the combined teachings Plata-Salaman and Moormann because neither of these two references teaches or suggests an administrative form for rapid release.

In response to this allegation, the Examiner respectfully disagrees and maintains that the Plata-Salaman and Moormann references, as discussed above, clearly teach and suggest the administration of galanthamine in a rapid release format as defined and claimed by Applicants, namely oral (e.g. buccal) and nasal forms. The limitations of claims 8 and 9 are simply directed to apparatus limitations for administering the drug in nasal form. The teachings of Samuels are directed to a nasal adaptor used in conjunction with a pressurized valved dispenser (col. 1, lines 15-17) in order to overcome the inefficient and unsatisfactory short-comings of *previous* nasal spray bottle devices (col. 1, lines 18-25 and 36-47) [*emphasis added*].

Lastly, concerning Applicants' assertion that the reference teaches away from the use of flexible plastic containers, the Examiner respectfully directs Applicants' their own remarks stating that they acknowledge that "Samuels teaches pressurized, valved, dispensers which may be made of flexible plastic, *see* column 2, lines 33-35". Said remark was made in response to the Examiner pointing out that Samuels clearly teaches a preference for flexible plastic material (i.e. "I have found that my invention *functions best* when made with flexible plastic") [*emphasis added*].

For these reasons, Applicants' arguments are found unpersuasive. Said rejection is therefore **maintained**.

REQUEST FOR REJOINDER

Applicants' request to rejoin the non-elected method claims has been considered. However, as all claims currently under consideration remain rejected (e.g. the elected product claims are not in condition for allowance), rejoinder is denied at this time.

CONCLUSION

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615